

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:sssptal617srh

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 SEP 09 ACD predicted properties enhanced in REGISTRY/ZREGISTRY
NEWS 4 OCT 03 MATHDI removed from STN
NEWS 5 OCT 04 CA/Caplus-Canadian Intellectual Property Office (CIPO) added
to core patent offices
NEWS 6 OCT 13 New CAS Information Use Policies Effective October 17, 2005
NEWS 7 OCT 17 STN(R) AnaVist(TM), Version 1.01, allows the export/download
of Caplus documents for use in third-party analysis and
visualization tools
NEWS 8 OCT 27 Free KWIC format extended in full-text databases
NEWS 9 OCT 27 DIOGENES content streamlined
NEWS 10 OCT 27 EPFULL enhanced with additional content
NEWS 11 NOV 14 CA/Caplus - Expanded coverage of German academic research
NEWS 12 NOV 30 REGISTRY/ZREGISTRY on STN(R) enhanced with experimental
spectral property data
NEWS 13 DEC 05 CASREACT(R) - Over 10 million reactions available
NEWS 14 DEC 14 2006 MeSH terms loaded in MEDLINE/LMEDLINE
NEWS 15 DEC 14 2006 MeSH terms loaded for MEDLINE file segment of TOXCENTER
NEWS 16 DEC 14 CA/Caplus to be enhanced with updated IPC codes
NEWS 17 DEC 16 MARPATprev will be removed from STN on December 31, 2005

NEWS EXPRESS DECEMBER 02 CURRENT VERSION FOR WINDOWS IS V8.01,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 02 DECEMBER 2005.
V8.0 USERS CAN OBTAIN THE UPGRADE TO V8.01 AT
<http://download.cas.org/express/v8.0-Discover/>

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

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of commercial gateways or other similar uses is prohibited and may
result in loss of user privileges and other penalties.

* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 16:14:55 ON 19 DEC 2005

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
FULL ESTIMATED COST	ENTRY	SESSION
	0.21	0.21

FILE 'STNGUIDE' ENTERED AT 16:14:59 ON 19 DEC 2005
 USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
 COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
 AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: Dec 16, 2005 (20051216/UP).

=> FIL HOME

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
FULL ESTIMATED COST	ENTRY	SESSION
	0.06	0.27

FILE 'HOME' ENTERED AT 16:15:04 ON 19 DEC 2005

=> fil capl

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
FULL ESTIMATED COST	ENTRY	SESSION
	0.21	0.48

FILE 'CAPLUS' ENTERED AT 16:15:09 ON 19 DEC 2005
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 19 Dec 2005 VOL 143 ISS 26
 FILE LAST UPDATED: 18 Dec 2005 (20051218/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

=> s us5385929/pn
 L1 1 US5385929/PN

=> sel rn
 E1 THROUGH E21 ASSIGNED

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
FULL ESTIMATED COST	ENTRY	SESSION
	2.42	2.90

FILE 'REGISTRY' ENTERED AT 16:15:24 ON 19 DEC 2005
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
 COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 18 DEC 2005 HIGHEST RN 870123-57-2
DICTIONARY FILE UPDATES: 18 DEC 2005 HIGHEST RN 870123-57-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

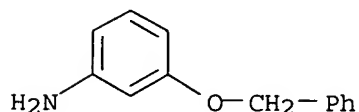
=> s el-21

1 100-52-7/BI
 (100-52-7/RN)
1 125995-13-3/BI
 (125995-13-3/RN)
1 1484-26-0/BI
 (1484-26-0/RN)
1 163217-66-1/BI
 (163217-66-1/RN)
1 163217-67-2/BI
 (163217-67-2/RN)
1 163217-68-3/BI
 (163217-68-3/RN)
1 163217-69-4/BI
 (163217-69-4/RN)
1 163217-70-7/BI
 (163217-70-7/RN)
1 163217-71-8/BI
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1 163217-72-9/BI
 (163217-72-9/RN)
1 163217-73-0/BI
 (163217-73-0/RN)
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 (163217-75-2/RN)
1 163217-76-3/BI
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1 163217-77-4/BI
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1 20012-63-9/BI

(20012-63-9/RN)
 1 42558-54-3/BI
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 1 459-57-4/BI
 (459-57-4/RN)
 1 57-88-5/BI
 (57-88-5/RN)
 1 6373-46-2/BI
 (6373-46-2/RN)
 1 9028-35-7/BI
 (9028-35-7/RN)
 L2 21 (100-52-7/BI OR 125995-13-3/BI OR 1484-26-0/BI OR 163217-66-1/BI
 OR 163217-67-2/BI OR 163217-68-3/BI OR 163217-69-4/BI OR 163217-
 -70-7/BI OR 163217-71-8/BI OR 163217-72-9/BI OR 163217-73-0/BI
 OR 163217-74-1/BI OR 163217-75-2/BI OR 163217-76-3/BI OR 163217-
 77-4/BI OR 20012-63-9/BI OR 42558-54-3/BI OR 459-57-4/BI OR
 57-88-5/BI OR 6373-46-2/BI OR 9028-35-7/BI)

=> d scan

L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN Benzenamine, 3-(phenylmethoxy) - (9CI)
 MF C13 H13 N O
 CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

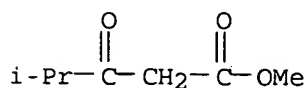
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):20

L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN Reductase, hydroxymethylglutaryl coenzyme A (reduced nicotinamide adenine
 dinucleotide phosphate) (9CI)
 MF Unspecified
 CI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

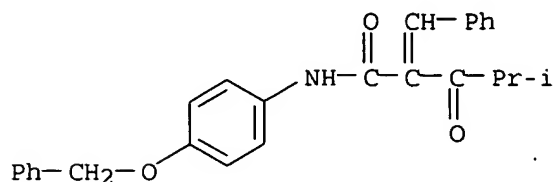
L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN Pentanoic acid, 4-methyl-3-oxo-, methyl ester (9CI)
 MF C7 H12 O3



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN

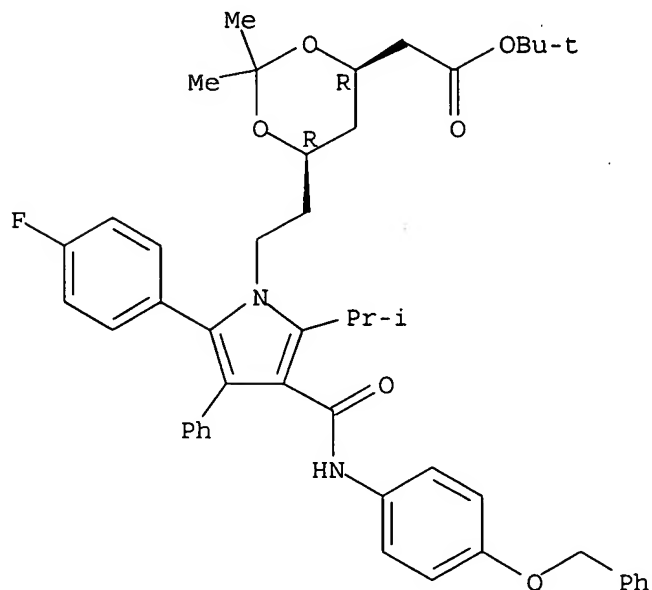
IN Pentanamide, 4-methyl-3-oxo-N-[4-(phenylmethoxy)phenyl]-2-(phenylmethylene)- (9CI)
 MF C26 H25 N O3



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN 1,3-Dioxane-4-acetic acid, 6-[2-[2-(4-fluorophenyl)-5-(1-methylethyl)-3-phenyl-4-[[[4-(phenylmethoxy)phenyl]amino]carbonyl]-1H-pyrrol-1-yl]ethyl]-2,2-dimethyl-, 1,1-dimethylethyl ester, (4R,6R)- (9CI)
 MF C47 H53 F N2 O6

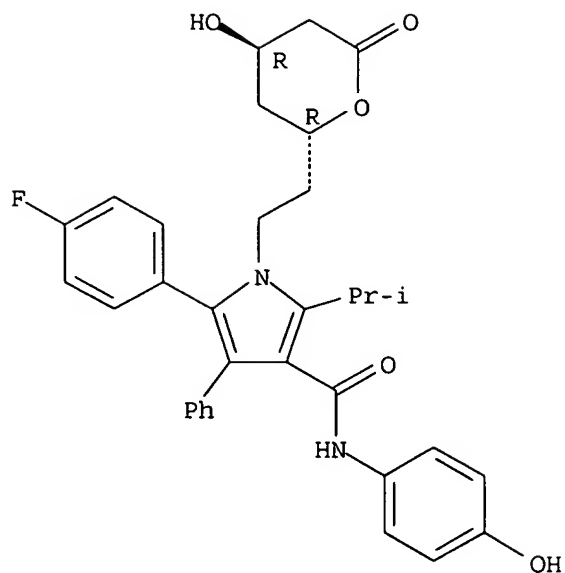
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN 1H-Pyrrole-3-carboxamide, 5-(4-fluorophenyl)-N-(4-hydroxyphenyl)-2-(1-methylethyl)-4-phenyl-1-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]- (9CI)
 MF C33 H33 F N2 O5

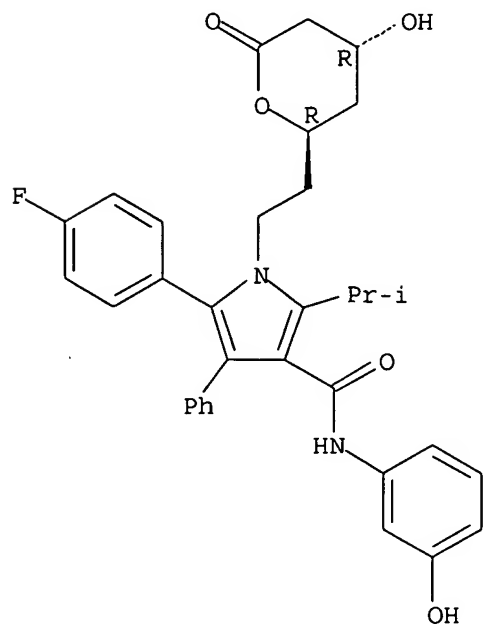
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN 1H-Pyrrole-3-carboxamide, 5-(4-fluorophenyl)-N-(3-hydroxyphenyl)-2-(1-methylethyl)-4-phenyl-1-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-, (2R-trans)- (9CI)
 MF C33 H33 F N2 O5

Absolute stereochemistry.

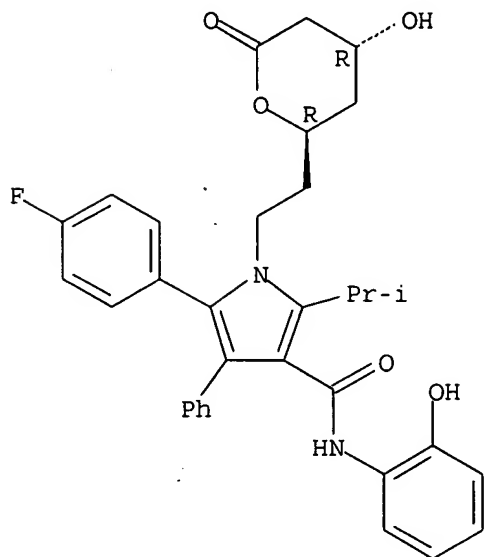


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN

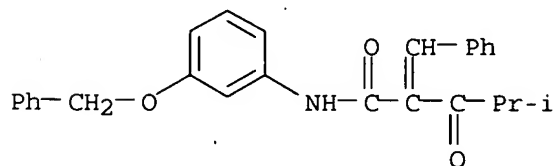
IN 1H-Pyrrole-3-carboxamide, 5-(4-fluorophenyl)-N-(2-hydroxyphenyl)-2-(1-methylethyl)-4-phenyl-1-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl] - (9CI)
 MF C33 H33 F N2 O5

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

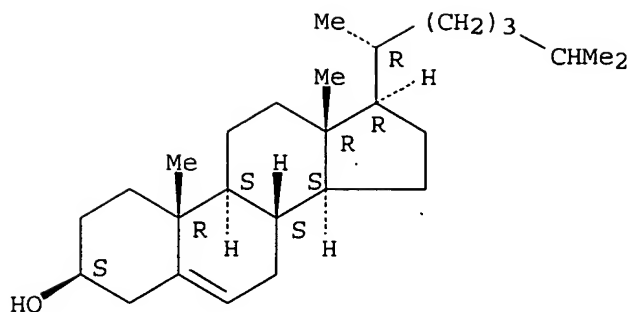
L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN Pentanamide, 4-methyl-3-oxo-N-[3-(phenylmethoxy)phenyl]-2-(phenylmethylene) - (9CI)
 MF C26 H25 N O3



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

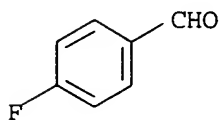
L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN Cholest-5-en-3-ol (3β) - (9CI)
 MF C27 H46 O
 CI COM

Absolute stereochemistry.



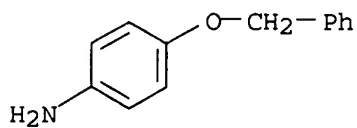
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN Benzaldehyde, 4-fluoro- (9CI)
 MF C7 H5 F O
 CI COM



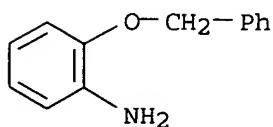
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN Benzenamine, 4-(phenylmethoxy)- (9CI)
 MF C13 H13 N O
 CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

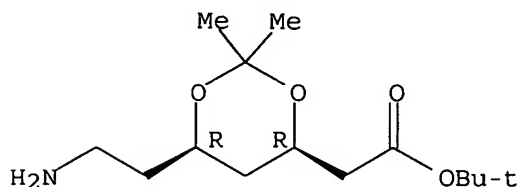
L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN Benzenamine, 2-(phenylmethoxy)- (9CI)
 MF C13 H13 N O
 CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

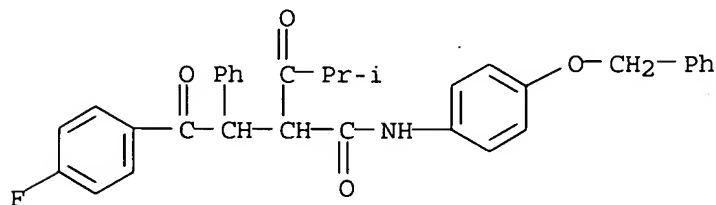
L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN 1,3-Dioxane-4-acetic acid, 6-(2-aminoethyl)-2,2-dimethyl-,
 1,1-dimethylethyl ester, (4R,6R)- (9CI)
 MF C14 H27 N O4
 CI COM

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

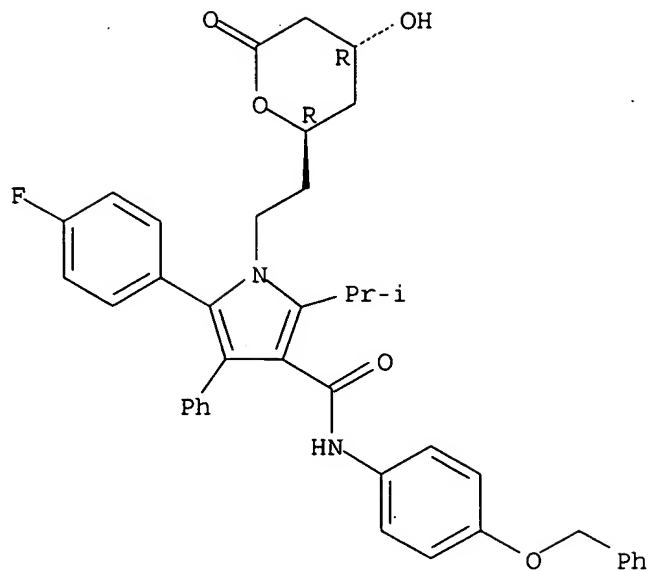
L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN Benzenebutanamide, 4-fluoro- α -(2-methyl-1-oxopropyl)- γ -oxo-
 β -phenyl-N-[4-(phenylmethoxy)phenyl]- (9CI)
 MF C33 H30 F N O4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN 1H-Pyrrole-3-carboxamide, 5-(4-fluorophenyl)-2-(1-methylethyl)-4-phenyl-N-
 [4-(phenylmethoxy)phenyl]-1-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-
 yl)ethyl]-, (2R-trans)- (9CI)
 MF C40 H39 F N2 O5

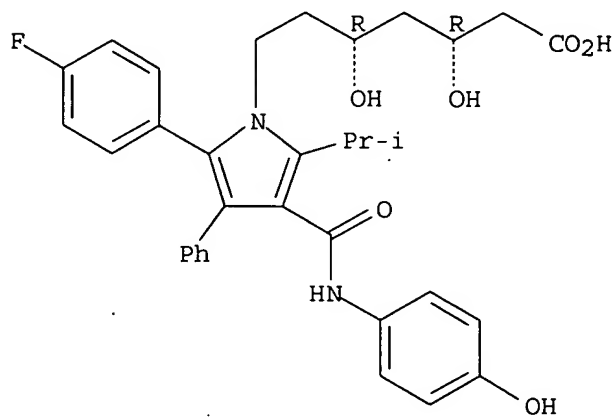
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN 1H-Pyrrole-1-heptanoic acid, 2-(4-fluorophenyl)- β,δ -dihydroxy-4-
 [[(4-hydroxyphenyl)amino]carbonyl]-5-(1-methylethyl)-3-phenyl-, monosodium
 salt, ($\beta R, \delta R$)- (9CI)
 MF C33 H35 F N2 O6 . Na

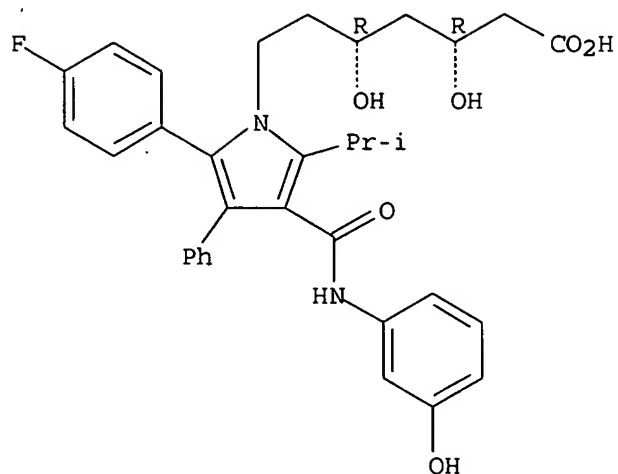
Absolute stereochemistry.



● Na

L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN 1H-Pyrrole-1-heptanoic acid, 2-(4-fluorophenyl)- β,δ -dihydroxy-4-
 [[(3-hydroxyphenyl)amino]carbonyl]-5-(1-methylethyl)-3-phenyl-, monosodium
 salt, [R-(R*,R*)]- (9CI)
 MF C33 H35 F N2 O6 . Na

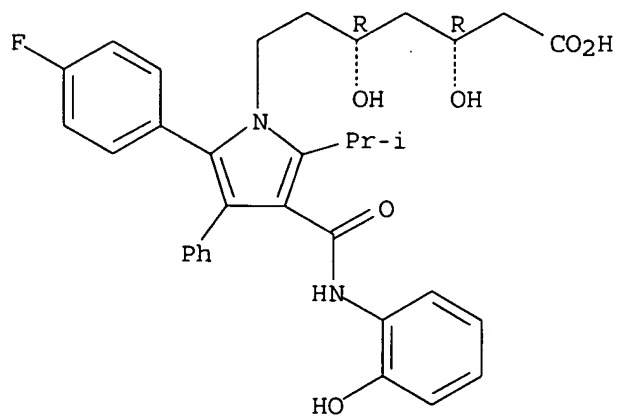
Absolute stereochemistry.



● Na

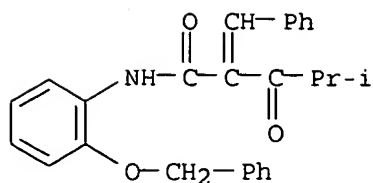
L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN 1H-Pyrrole-1-heptanoic acid, 2-(4-fluorophenyl)- β , δ -dihydroxy-4-
 [[(2-hydroxyphenyl)amino]carbonyl]-5-(1-methylethyl)-3-phenyl-, monosodium
 salt, (β R, δ R)- (9CI)
 MF C33 H35 F N2 O6 . Na

Absolute stereochemistry.



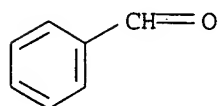
● Na

L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN Pentanamide, 4-methyl-3-oxo-N-[2-(phenylmethoxy)phenyl]-2-
 (phenylmethylene)- (9CI)
 MF C26 H25 N O3



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 21 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
 IN Benzaldehyde (7CI, 8CI, 9CI)
 MF C7 H6 O
 CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

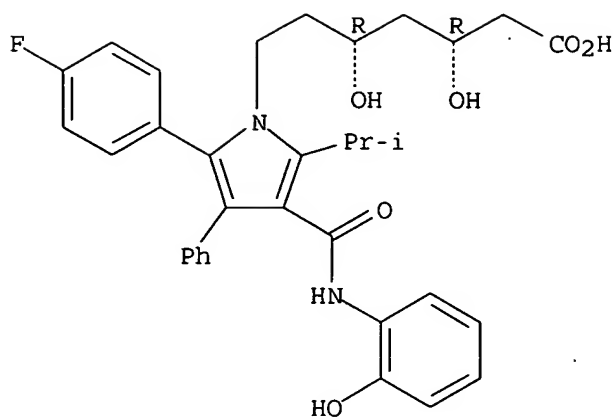
ALL ANSWERS HAVE BEEN SCANNED

=> s l2 and C33 H35 F N2 O6 . Na/mf
 5 C33 H35 F N2 O6 . NA/MF
 L3 3 L2 AND C33 H35 F N2 O6 . NA/MF

=> d tot

L3 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN
 RN 163217-75-2 REGISTRY
 ED Entered STN: 24 May 1995
 CN 1H-Pyrrole-1-heptanoic acid, 2-(4-fluorophenyl)-β,δ-dihydroxy-4-
 [[(2-hydroxyphenyl) amino] carbonyl] -5-(1-methylethyl)-3-phenyl-, monosodium
 salt, (βR,δR)- (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN 1H-Pyrrole-1-heptanoic acid, 2-(4-fluorophenyl)-β,δ-dihydroxy-4-
 [[(2-hydroxyphenyl) amino] carbonyl] -5-(1-methylethyl)-3-phenyl-, monosodium
 salt, [R-(R*,R*)]-
 OTHER NAMES:
 CN [3R,5R]-2-(4-Fluorophenyl)-β,δ-dihydroxy-5-(1-methylethyl)-3-
 phenyl-4-[[(2-hydroxyphenyl) amino] carbonyl] -1H-pyrrole-1-heptanoic acid
 sodium salt
 FS STEREOSEARCH
 MF C33 H35 F N2 O6 . Na
 SR CA
 LC STN Files: CA, CAPLUS, USPATFULL
 CRN (214217-86-4)

Absolute stereochemistry.

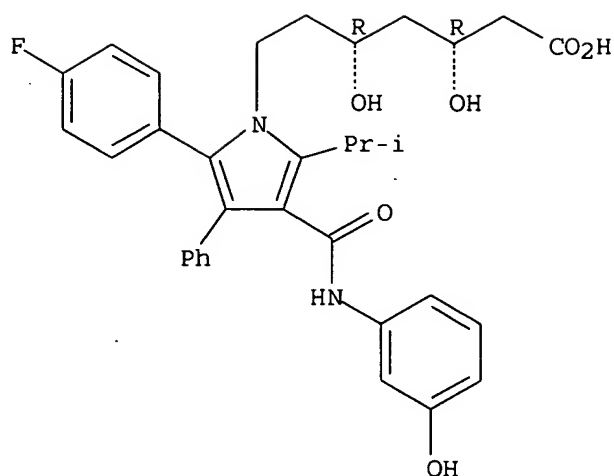


● Na

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN
RN **163217-73-0** REGISTRY
ED Entered STN: 24 May 1995
CN 1H-Pyrrole-1-heptanoic acid, 2-(4-fluorophenyl)- β , δ -dihydroxy-4-
[[(3-hydroxyphenyl)amino]carbonyl]-5-(1-methylethyl)-3-phenyl-, monosodium
salt, [R-(R*,R*)]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN [3R,5R]-2-(4-Fluorophenyl)- β , δ -dihydroxy-5-(1-methylethyl)-3-
phenyl-4-[(3-hydroxyphenylamine)carbonyl]-1H-pyrrole-1-heptanoic acid
sodium salt
FS STEREOSEARCH
MF **C33 H35 F N2 O6 . Na**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
CRN (769896-65-3)

Absolute stereochemistry.



● Na

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN

RN 163217-71-8 REGISTRY

ED Entered STN: 24 May 1995

CN 1H-Pyrrole-1-heptanoic acid, 2-(4-fluorophenyl)-β,δ-dihydroxy-4-
[[(4-hydroxyphenyl) amino] carbonyl] -5-(1-methylethyl)-3-phenyl-, monosodium
salt, (βR,δR)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Pyrrole-1-heptanoic acid, 2-(4-fluorophenyl)-β,δ-dihydroxy-4-
[[(4-hydroxyphenyl) amino] carbonyl] -5-(1-methylethyl)-3-phenyl-, monosodium
salt, [R-(R*,R*)]-

OTHER NAMES:

CN [3R,5R]-2-(4-Fluorophenyl)-β,δ-dihydroxy-5-(1-methylethyl)-3-
phenyl-4-[(4-hydroxyphenylamino) carbonyl]-1H-pyrrole-1-heptanoic acid
sodium salt

FS STEREOSEARCH

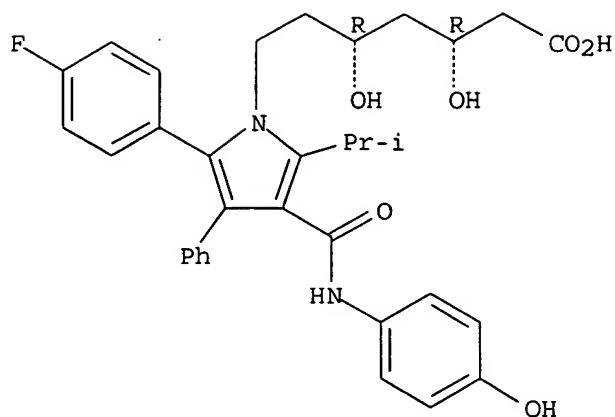
MF C33 H35 F N2 O6 . Na

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

CRN (214217-88-6)

Absolute stereochemistry.



● Na

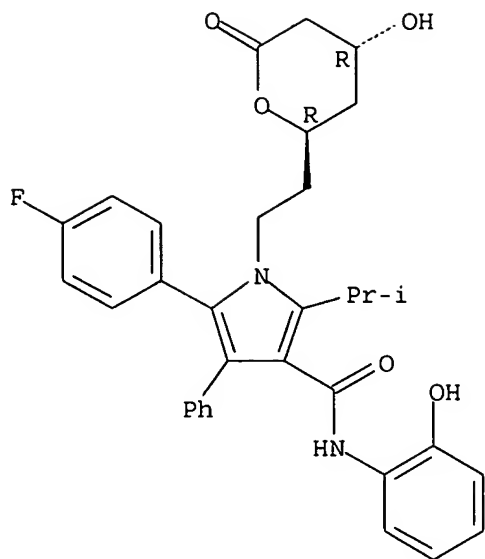
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s 12 and C33 H33 F N2 O5/mf
29 C33 H33 F N2 O5/MF
L4 3 L2 AND C33 H33 F N2 O5/MF

=> d tot

L4 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN
RN **163217-74-1** REGISTRY
ED Entered STN: 24 May 1995
CN 1H-Pyrrole-3-carboxamide, 5-(4-fluorophenyl)-N-(2-hydroxyphenyl)-2-(1-methylethyl)-4-phenyl-1-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Pyrrole-3-carboxamide, 5-(4-fluorophenyl)-N-(2-hydroxyphenyl)-2-(1-methylethyl)-4-phenyl-1-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-, (2R-trans)-
OTHER NAMES:
CN (2R-trans)-5-(4-Fluorophenyl)-2-(1-methylethyl)-N-(2-hydroxyphenyl)-4-phenyl-1-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1H-pyrrole-3-carboxamide
FS STEREOSEARCH
DR 314059-12-6
MF **C33 H33 F N2 O5**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9 REFERENCES IN FILE CA (1907 TO DATE)

9 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L4 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN

RN 163217-72-9 REGISTRY

ED Entered STN: 24 May 1995

CN 1H-Pyrrole-3-carboxamide, 5-(4-fluorophenyl)-N-(3-hydroxyphenyl)-2-(1-methylethyl)-4-phenyl-1-[2-((2R-trans)-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-, (2R-trans)- (9CI) (CA INDEX NAME)

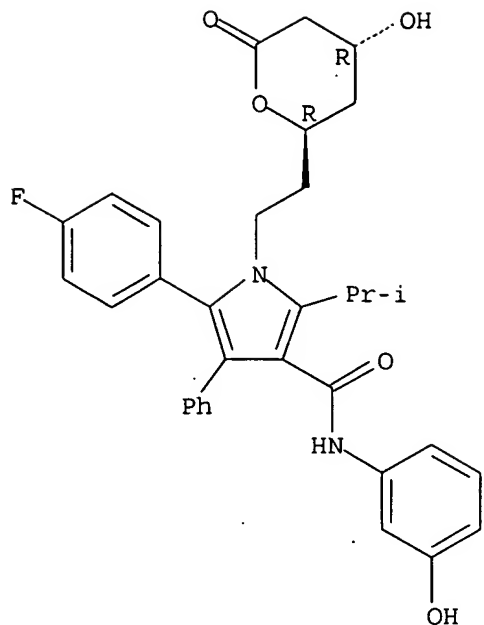
FS STEREOSEARCH

MF C33 H33 F N2 O5

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L4 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN

RN 163217-70-7 REGISTRY

ED Entered STN: 24 May 1995

CN 1H-Pyrrole-3-carboxamide, 5-(4-fluorophenyl)-N-(4-hydroxyphenyl)-2-(1-methylethyl)-4-phenyl-1-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Pyrrole-3-carboxamide, 5-(4-fluorophenyl)-N-(4-hydroxyphenyl)-2-(1-methylethyl)-4-phenyl-1-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-, (2R-trans)-

OTHER NAMES:

CN (2R-trans)-5-(4-Fluorophenyl)-2-(1-methylethyl)-N-(4-hydroxyphenyl)-4-phenyl-1-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)-ethyl]-1H-pyrrole-3-carboxamide

FS STEREOSEARCH

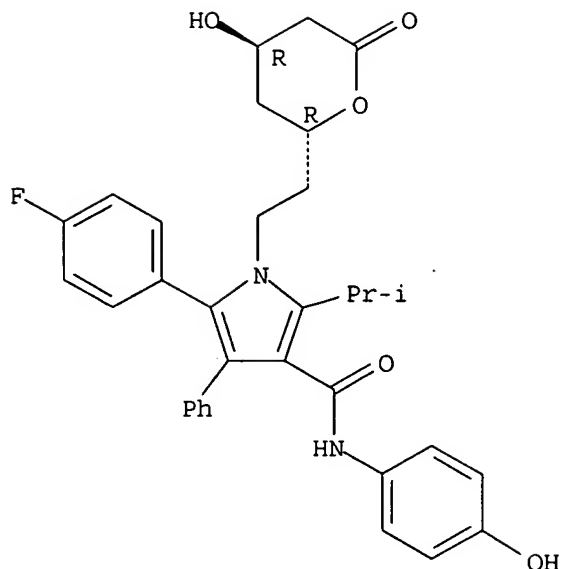
DR 314059-11-5

MF C33 H33 F N2 O5

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

6 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> fil medl capl uspatf wpids
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
21.96	24.86

FULL ESTIMATED COST

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=> s 14
L5 10 L4

=> dup rem 15
PROCESSING COMPLETED FOR L5
L6 9 DUP REM L5 (1 DUPLICATE REMOVED)

=> d ibib abs 5-9

L6 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:176893 CAPLUS
DOCUMENT NUMBER: 132:308162
TITLE: Synthesis of deuterium-labeled atorvastatin and its
metabolites for use as internal standards in a
LC/MS/MS method developed for quantitation of the drug
and its metabolites in human serum

AUTHOR(S) : Chen, Bang-Chi; Sundeen, Joseph E.; Guo, Peng;
Bednarz, Mark S.; Hangeland, Jon J.; Ahmed, Syed Z.;
Jemal, Mohammed
CORPORATE SOURCE: Discovery Chemistry, Bristol-Myers Squibb
Pharmaceutical Research Institute, Princeton, NJ,
08543-4000, USA
SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals
(2000), 43(3), 261-270
CODEN: JLCRD4; ISSN: 0362-4803
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB D5-labeled isotopomers of atorvastatin, atorvastatin lactone and its
hydroxy metabolites were synthesized as internal stds. for use in a
LC/MS/MS method developed for the simultaneous quant. determination of
atorvastatin and its hydroxy metabolites in human serum. D5-Atorvastatin
and d5-atorvastatin lactone were prepared from d5-aniline whereas their
corresponding hydroxy metabolites were synthesized using d5-benzaldehyde.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:373479 CAPLUS

DOCUMENT NUMBER: 131:164924

TITLE: Quantitation of the acid and lactone forms of
atorvastatin and its biotransformation products in
human serum by high-performance liquid chromatography
with electrospray tandem mass spectrometry.

AUTHOR(S) : Jemal, Mohammed; Ouyang, Zheng; Chen, Bang-Chi; Teitz,
Deborah

CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research
Institute, New Brunswick, NJ, 08903-0191, USA

SOURCE: Rapid Communications in Mass Spectrometry (1999),
13(11), 1003-1015

CODEN: RCMSEF; ISSN: 0951-4198

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A method for simultaneous quantitation of both the acid and lactone forms
of atorvastatin, a new synthetic inhibitor of HMG-CoA reductase that is
being marketed for the treatment of high serum cholesterol, and both the
acid and lactone forms of its two biotransformation products,
2-hydroxyatorvastatin and 4-hydroxyatorvastatin, in human serum (a total
of six analytes) by high-performance liquid chromatog. with electrospray
tandem mass spectrometry was developed and validated. A deuterium labeled
analog was used as internal standard for each of the six analytes. Each point
of the calibration standard curve, which ranged from 0.5 to 200 ng/mL,
contained the six analytes at equal concns. Three groups of quality
control (QC) samples were used. In the first group, combination QC
samples contained all six analytes at equal concns. In the second group,
acid-only QC samples contained only the acid forms (i.e. three analytes)
at equal concns. In the third group, lactone-only QC samples contained
only the lactone forms (i.e. three analytes) at equal concns. After
adding the internal stds. to 0.5 mL of each standard and the QC sample kept at
4°C, the samples were acidified with sodium acetate buffer (pH 5.0)
and then extracted with Me tert-Bu ether. Detection was by pos. ion
electrospray tandem mass spectrometry using eight selected reaction
monitoring channels. The acid compds. were stable in human serum at room
temperature but the lactone compds. were unstable as they hydrolyzed rapidly to
their resp. acid forms. The conversion of the lactone compds. in both QC
and post-dose human serum samples was nearly complete after 24 h at room
temperature. The lactone compds. in serum could be stabilized by lowering the
working temperature to 4°C or lowering the serum pH to 6.0. The
acid-only and the lactone-only QC samples showed that, under the sample

processing conditions used, the degree of the hydrolysis of the lactone compds. or the lactonization of the acid compds. during the assay procedure was minimal (<5%). The intra-day C.V., inter-day C.V. and the deviations from the nominal concns. for all six analytes were within 15%, demonstrating good precision and accuracy. The required lower limit of quantitation (LLQ) of 0.5 ng/mL was achieved for each analyte.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:587216 CAPLUS

DOCUMENT NUMBER: 131:346095

TITLE: Grapefruit juice increases serum concentrations of atorvastatin and has no effect on pravastatin

AUTHOR(S): Lilja, Jari J.; Kivisto, Kari T.; Neuvonen, Pertti J.

CORPORATE SOURCE: Department of Clinical Pharmacology, University of Helsinki and Helsinki University Central Hospital, Helsinki, FIN-00290, Finland

SOURCE: Clinical Pharmacology & Therapeutics (St. Louis) (1999), 66(2), 118-127

CODEN: CLPTAT; ISSN: 0009-9236

PUBLISHER: Mosby, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: Grapefruit juice greatly increases the bioavailability of lovastatin and simvastatin. We studied the effect of grapefruit juice on the pharmacokinetics of atorvastatin and pravastatin. Methods: Two randomized, two-phase crossover studies were performed; study I with atorvastatin in 12 healthy volunteers and study II with pravastatin in 11 healthy volunteers. In both studies, volunteers took 200 mL double-strength grapefruit juice or water three times a day for 2 days. On day 3, each subject ingested a single 40 mg dose of atorvastatin (study I) or pravastatin (study II) with either 200 mL grape-fruit juice or water, and an addnl. 200 mL was ingested 1/2 h and 1 1/2 h later. In addition, subjects took 200 mL grapefruit juice or water three times a day on days 4 and 5 in study I. In study I, serum concns. of atorvastatin acid, atorvastatin lactone, 2-hydroxyatorvastatin acid, 2-hydroxyatorvastatin lactone, and active and total 3-hydroxy-3-methylglutaryl CoA (HMG-CoA) reductase inhibitors were measured up to 72 h. In study II, pravastatin, pravastatin lactone, and active and total HMG-CoA reductase inhibitors were measured up to 24 h. Results: Grapefruit juice increased the area under the serum concentration-time curve of atorvastatin acid from time zero to 72 h [AUC(0-72)] 2.5-fold ($P < .01$), whereas the peak serum concentration (C_{max}) was not significantly changed. The time of the peak concentration (t_{max}) and

the

elimination half-life ($t_{1/2}$) of atorvastatin acid were increased ($P < .01$). The AUC(0-72) of atorvastatin lactone was increased 3.3-fold ($P < .01$) and the C_{max} 2.6-fold ($P < .01$) by grapefruit juice, and the t_{max} and $t_{1/2}$ were also increased ($P < .05$). Grapefruit juice decreased the C_{max} ($P < .001$) and AUC(0-72) ($P < .001$) of 2-hydroxyatorvastatin acid and increased its t_{max} and $t_{1/2}$ ($P < .01$). Grapefruit juice also decreased the C_{max} ($P < .001$) and AUC(0-72) ($P < .05$) of 2-hydroxyatorvastatin lactone. The AUC(0-72) values of active and total HMG-CoA reductase inhibitors were increased 1.3-fold ($P < .05$) and 1.5-fold ($P < .01$), resp., by grapefruit juice. In study II, the only significant change observed in the pharmacokinetics of pravastatin was prolongation of the t_{max} of active HMG-CoA reductase inhibitors by grapefruit juice ($P < .05$). Conclusions: Grapefruit juice significantly increased serum concns. of atorvastatin acid, atorvastatin lactone, and active and total HMG-CoA reductase inhibitors, probably by decreasing CYP3A4-mediated first-pass metabolism of atorvastatin in the small intestine. On the other hand, grapefruit juice had no effect on the pharmacokinetics of pravastatin. Concomitant use of atorvastatin and at least large amts. of grapefruit juice should be avoided, or the dose of atorvastatin should be reduced accordingly.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:532807 CAPLUS

DOCUMENT NUMBER: 129:285588

TITLE: Effect of itraconazole on the pharmacokinetics of atorvastatin

AUTHOR(S): Kantola, Teemu; Kivistoe, Kari T.; Neuvonen, Pertti J.

CORPORATE SOURCE: the Department of Clinical Pharmacology, University of Helsinki and Helsinki University Central Hospital, Helsinki, Finland

SOURCE: Clinical Pharmacology and Therapeutics (St. Louis) (1998), 64(1), 58-65

CODEN: CLPTAT; ISSN: 0009-9236

PUBLISHER: Mosby, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Itraconazole, a potent inhibitor of CYP3A4, increases the risk of skeletal muscle toxicity of some 3-hydroxy-3-methylglutaryl CoA (HMG-CoA) reductase inhibitors by increasing their blood serum concns. The effect of itraconazole was characterized on the pharmacokinetics of atorvastatin, a new HMG-CoA reductase inhibitor that is metabolized at least in part by CYP3A4. Healthy took 200 mg itraconazole or matched placebo orally once daily for 4 days. On day 4, 40 mg atorvastatin was administered orally, and a further dose of 200 mg itraconazole or placebo was taken 24 h after atorvastatin intake. Serum concns. of atorvastatin acid, atorvastatin lactone, 2-hydroxyatorvastatin acid and lactone, 4-hydroxyatorvastatin acid and lactone, active and total HMG-CoA reductase inhibitors, itraconazole, and hydroxyitraconazole were measured ≤ 72 h. Itraconazole increased the area under the concentration-time curve from time 0

to 72 h [AUC(0-72)] and the elimination half-life of atorvastatin acid about 3-fold, whereas the peak serum concentration was not changed. The AUC(0-72) of atorvastatin lactone was increased about 4-fold, and the peak serum concentration

and half-life were increased more than 2-fold. Itraconazole decreased the peak serum concentration and AUC(0-72) of 2-hydroxyatorvastatin acid and 2-hydroxyatorvastatin lactone. Itraconazole increased the half-life of 2-hydroxyatorvastatin lactone. The AUC(0-72) values of active and total HMG-CoA reductase inhibitors were increased 1.6-fold and 1.7-fold, resp. Thus, itraconazole has a significant interaction with atorvastatin. The mechanism of increased serum concns. of atorvastatin and HMG-CoA reductase inhibitors is inhibition of CYP3A4-mediated metabolism of atorvastatin and its metabolites by itraconazole. Concomitant use of itraconazole and other potent inhibitors of CYP3A4 with atorvastatin should be avoided or the dose of atorvastatin should be reduced accordingly.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 1995:403387 CAPLUS

DOCUMENT NUMBER: 122:314449

TITLE: [(Hydroxyphenylamino)carbonyl]pyrroles useful in treating hypercholesterolemia

INVENTOR(S): Bjorge, Susan M.; Black, Ann E.; Roth, Bruce D.; Woolf, Thomas

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: U.S., 8 pp.

CODEN: USXXAM

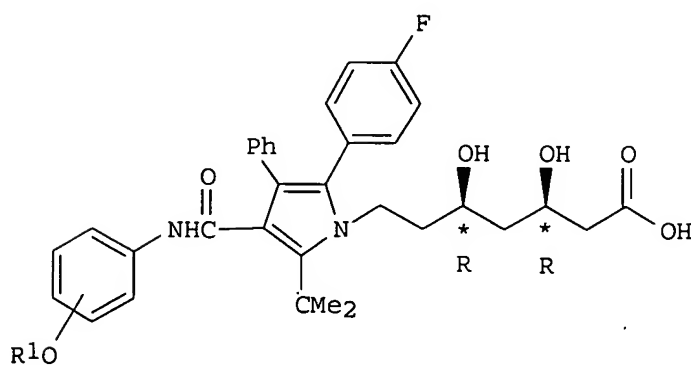
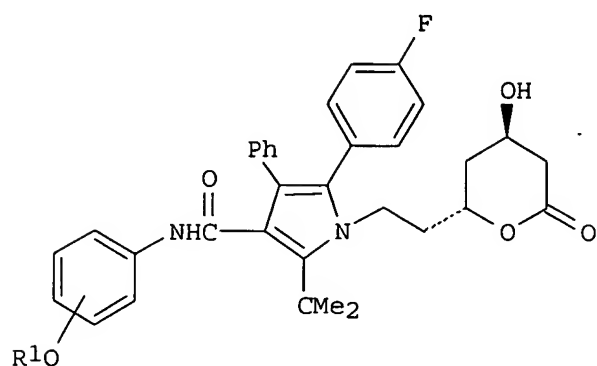
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5385929	A	19950131	US 1994-238120	19940504
JP 07304735	A2	19951121	JP 1995-107719	19950502
JP 3316661	B2	20020819		
EP 680963	A1	19951108	EP 1995-106676	19950503
EP 680963	B1	20011121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 209203	E	20011215	AT 1995-106676	19950503
PT 680963	T	20020531	PT 1995-106676	19950503
ES 2168318	T3	20020616	ES 1995-106676	19950503
PRIORITY APPLN. INFO.:			US 1994-238120	A 19940504
OTHER SOURCE(S):			MARPAT 122:314449	
GI				



AB A title compound of the formula I where R1 is hydrogen or a hydroxy protecting group and solvates thereof, or the open chain form of the formula II and the pharmaceutically acceptable salts and solvates thereof inhibits cholesterol biosynthesis, and thus is useful in treating hypercholesterolemia. The compds. of the invention have shown excellent activity in inhibiting cholesterol biosynthesis by inhibiting the HMG-CoA reductase enzyme: at 10 ng/mL, inhibition of 51-100%; at 1 ng/mL, from 49 to 100%.

=> fil reg

COST IN U.S. DOLLARS

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

CA SUBSCRIBER PRICE

SINCE FILE

ENTRY

27.60

SINCE FILE

ENTRY

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TOTAL

SESSION

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TOTAL

SESSION

-3.65

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<http://www.cas.org/ONLINE/UG/regprops.html>

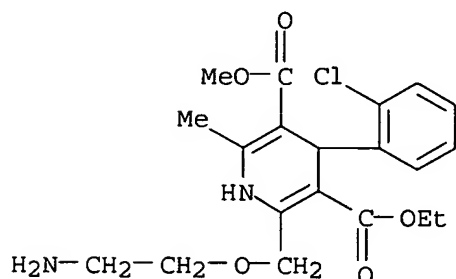
=> s amlodiine/cn
L7 0 AMLODIINE/CN

=> s amlodipine/cn
L8 1 AMLODIPINE/CN

=> d

L8 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 88150-42-9 REGISTRY
ED Entered STN: 16 Nov 1984
CN 3,5-Pyridinedicarboxylic acid, 2-[(2-aminoethoxy)methyl]-4-(2-
chlorophenyl)-1,4-dihydro-6-methyl-, 3-ethyl 5-methyl ester (9CI) (CA
INDEX NAME)
OTHER NAMES:
CN 2-[(2-Aminoethoxy)methyl]-4-(2-chlorophenyl)-3-(ethoxycarbonyl)-5-
(methoxycarbonyl)-6-methyl-1,4-dihydropyridine
CN **Amlodipine**
CN Pelmec
CN Racemic Amlodipine
FS 3D CONCORD
DR 103069-18-7
MF C20 H25 Cl N2 O5
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,

CHEMLIST, CIN, CSCHM, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IMSPATENTS,
 IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH,
 SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
 (*File contains numerically searchable property data)
 Other Sources: WHO



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1536 REFERENCES IN FILE CA (1907 TO DATE)
 29 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 1539 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> FIL MEDL CAPL USPATF WPIDS
 COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
11.47	63.93

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE ENTRY	TOTAL SESSION
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=> s 18
 L9 3347 L8

=> s hypercholesterolem? or dyslipidem? or cholesterol?
 L10 390202 HYPERCHOLESTEROLEM? OR DYSLIPIDEM? OR CHOLESTEROL?

=> s 19 and 110
 L11 267 L9 AND L10

=> s 19 (s) 110
 L12 17 L9 (S) L10

=> dup rem 112

PROCESSING COMPLETED FOR L12

L13 17 DUP REM L12 (0 DUPLICATES REMOVED)

=> d ibib abs 15-17

L13 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:2114 CAPLUS

DOCUMENT NUMBER: 124:135111

TITLE: Relationship between body mass index (BMI) and changes in plasma total and HDL-cholesterol levels during treatment of hypertension in African patients

AUTHOR(S): Ahaneku, Joseph Eberendu; Agbedana, Olu Emmanuel; Taylor, Oladunni Grace

CORPORATE SOURCE: Teaching Hospital Nnewi, Nnamdi Azikiwe University, Nnewi, Nigeria

SOURCE: Acta Medica Okayama (1995), 49(5), 267-70

CODEN: AMOKAG; ISSN: 0386-300X

PUBLISHER: Okayama University Medical School

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Eighty-one adult Nigerians with essential hypertension were randomly allocated to receive doxazosin, hydrochlorothiazide/amiloride, or amlodipine. In each group, the patients were further classified as obese and non-obese, and total cholesterol as well as high density lipoprotein (HDL) cholesterol was determined before and after the 3-mo treatment period. The total cholesterol level was significantly reduced in the non-obese patients, but did not show any significant change in the obese patients after doxazosin therapy, indicating the beneficial effects of doxazosin therapy in non-obese patients. The levels of total cholesterol increased and HDL cholesterol decreased in both the obese and the non-obese patients after hydrochlorothiazide/amiloride therapy. Amlodipine treatment did not cause any significant change in the total and HDL cholesterol levels in both the obese and non-obese patients. These findings are worthy of consideration by clinicians and researchers when selecting the most appropriate drug for antihypertensive pharmacotherapy.

L13 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1994:95390 CAPLUS

DOCUMENT NUMBER: 120:95390

TITLE: Cholesterol enrichment during dietary atherosclerosis alters smooth muscle plasma membrane width and structure: evidence for reversal by the 1,4-dihydropyridine amlodipine

AUTHOR(S): Mason, R. Preston; Herbette, Leo G.; Tulenko, Thomas N.

CORPORATE SOURCE: Dep. Radiol. Med. Biochem., Cent. Cardiovasc. Membrane Res., Farmington, CT, 06030, USA

SOURCE: Medical Science Symposia Series (1993), 3(Calcium Antagonists), 149-55

CODEN: MSSYEI; ISSN: 0928-9550

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cholesterol enrichment in smooth muscle cell plasma membrane has been associated with the pathobiology of atherosclerosis. The molecular interactions of amlodipine vs. other dihydropyridine calcium channel blockers with cholesterol enriched model and biological membranes was examined. Amlodipine reverses the lipid ordering effect of cholesterol, resulting in a decreased membrane bilayer width. The data may provide a mechanism for amlodipine's potential anti-atherosclerotic effect.

L13 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:563343 CAPLUS

DOCUMENT NUMBER: 117:163343

TITLE: Cholesterol alters the binding of calcium channel

blockers to the membrane lipid bilayer
AUTHOR(S): Mason, R. Preston; Moiesey, Donna M.; Shajenko, Lydia
CORPORATE SOURCE: Health Cent., Univ. Connecticut, Farmington, CT,
06030, USA
SOURCE: Molecular Pharmacology (1992), 41(2), 315-21
CODEN: MOPMA3; ISSN: 0026-895X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB X-ray diffraction and equilibrium binding techniques were used to study the effect of cholesterol on membrane binding of the charged 1,4-dihydropyridine (DHP) Ca²⁺ channel antagonist amlodipine and uncharged isradipine, nimodipine, and nitrendipine. Increases in membrane cholesterol content resulted in a marked decrease in DHP binding to cardiac phospholipid membranes, as expressed by the equilibrium partition coefficient (K_p[mem]). Between a 0:1 and 0.3:1 cholesterol to phospholipid mole ratio, the K_p[mem] values for isradipine, nimodipine, and nitrendipine decreased by >50%, whereas that for amlodipine decreased by only 10%. Electron d. profiles calculated from the x-ray diffraction data showed that the time-averaged locations for the DHPs and cholesterol in the membrane overlap, leading to the conclusion that the addition of cholesterol alters the lipid bilayer hydrocarbon core structure in a manner that makes drug partitioning into the membrane less energetically favorable. These data support the idea that drug interactions with the anisotropic membrane environment are complex and may be greatly influenced by cholesterol composition. This effect of cholesterol was also observed for phenylalkylamine (verapamil) and benzothiazepine (diltiazem) Ca²⁺ channel blockers. The DHP amlodipine had the highest membrane partition coefficient (K_p[mem] > 104) and the slowest rate of dissociation and was affected least by membrane cholesterol content. The combination of electrostatic and hydrophobic bonding between amlodipine and membrane phospholipid may explain the high affinity of this drug for the membrane bilayer with normal and elevated cholesterol. The results of this study show that cholesterol content differentially affects the membrane-binding properties of the charged DHP amlodipine, compared with other Ca²⁺ channel blockers. These data help explain the biol. distribution of these drugs and the distinct pharmacokinetics of amlodipine vs. other Ca²⁺ channel blockers.

=> d ibib abs 10-14

L13 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:514206 CAPLUS
DOCUMENT NUMBER: 139:391024
TITLE: Differential effects of amlodipine and atorvastatin treatment and their combination on atherosclerosis in ApoE*3-leiden transgenic mice
AUTHOR(S): Delsing, Dianne J. M.; Jukema, J. Wouter; van de Wiel, Mark A.; Emeis, Jef J.; van der Laarse, Arnoud; Havekes, Louis M.; Princen, Hans M. G.
CORPORATE SOURCE: Gaubius Laboratory, Neth.
SOURCE: Journal of Cardiovascular Pharmacology (2003), 42(1), 63-70
CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study was designed to investigate the potential antiatherosclerotic effects of the calcium antagonist amlodipine as compared with the HMG-CoA reductase inhibitor atorvastatin and the combination of both in ApoE*3-Leiden transgenic mice. Four groups of 15 ApoE*3-Leiden mice were put on a high-cholesterol diet. One group received 0.002% (wt/wt) amlodipine in the diet, which had no effect on plasma cholesterol levels. Another group received 0.01% (wt/wt) atorvastatin, resulting in a decrease of plasma cholesterol by 50% by a reduction in very low d. lipoprotein production

The combination group received both amlodipine and atorvastatin. After 28 wk, atherosclerosis in the aortic root was quantified. Treatment with amlodipine had no significant effect on atherosclerotic lesion area, whereas atorvastatin markedly reduced atherosclerosis by 77% compared with the control group. Atorvastatin also reduced inflammation markers. The combination of amlodipine and atorvastatin tended to reduce lesion area by 61% compared with the atorvastatin-only group; however, this effect did not reach statistical significance. Amlodipine treatment significantly reduced calcification in the lesions, whereas atorvastatin alone had no effect. The combination of amlodipine and atorvastatin resulted in a near absence of calcium deposits in the lesions. This study demonstrates that amlodipine treatment alone does not significantly reduce atherosclerotic lesion development. Atorvastatin was shown to have strong antiatherosclerotic effects, and cotreatment with amlodipine may potentiate the antiatherosclerotic effect of atorvastatin.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:122785 CAPLUS
DOCUMENT NUMBER: 136:161369
TITLE: Synergistic effect of amlodipine and atorvastatin
INVENTOR(S): Mason, R. Preston
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002011723	A1	20020214	WO 2001-US24209	20010803
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001083085	A5	20020218	AU 2001-83085	20010803
PRIORITY APPLN. INFO.: US 2000-223214P P 20000804				
WO 2001-US24209 W 20010803				

AB The combination of the antihypertensive calcium channel blocker amlodipine and lipid-lowering agent atorvastatin inhibits free cholesterol crystallization in atherosclerotic-like membranes. In addition, treatment with a combination of amlodipine and atorvastatin results in a synergistic effect on the release of NO from rabbit aorta endothelial cells.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:290837 CAPLUS
DOCUMENT NUMBER: 131:128461
TITLE: Increased NADH-oxidase-mediated superoxide production in the early stages of atherosclerosis: evidence for involvement of the renin-angiotensin system
AUTHOR(S): Warnholtz, Ascan; Nickenig, Georg; Schulz, Eberhard; Macharzina, Roland; Brasen, Jan Hinrich; Skatchkov, Mikhail; Heitzer, Thomas; Stasch, Johannes P.;

Griendling, Kathy K.; Harrison, David G.; Bohm, Michael; Meinertz, Thomas; Munzel, Thomas
CORPORATE SOURCE: Abteilung fur Kardiologie, Universitats-Krankenhaus Eppendorf, University of Hamburg, Hamburg, D-20246, Germany

SOURCE: Circulation (1999), 99(15), 2027-2033

CODEN: CIRCAZ; ISSN: 0009-7322

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Angiotensin II activates NAD(P)H-dependent oxidases via AT1-receptor stimulation, the most important vascular source of superoxide (O₂^{·-}). The AT1 receptor is upregulated in vitro by low-d. lipoprotein. The present study was designed to test whether hypercholesterolemia is associated with increased NAD(P)H-dependent vascular O₂^{·-} production and whether AT1-receptor blockade may inhibit this oxidase and in parallel improve endothelial dysfunction. Vascular responses were determined by isometric tension studies, and relative rates of vascular O₂^{·-} production were determined by use of chemiluminescence with lucigenin, a cypridina luciferin analog, and ESR studies. AT1-receptor mRNA was quantified by Northern anal., and AT1-receptor d. was measured by radioligand binding assays. Hypercholesterolemia was associated with impaired endothelium-dependent vasodilation and increased O₂^{·-} production in intact vessels. In vessel homogenates, we found a significant activation of NADH-driven O₂^{·-} production in both models of hyperlipidemia. Treatment of cholesterol-fed animals with the AT1-receptor antagonist Bay 10-6734 improved endothelial dysfunction, normalized vascular O₂^{·-} and NADH-oxidase activity, decreased macrophage infiltration, and reduced early plaque formation. In the setting of hypercholesterolemia, the aortic AT1 receptor mRNA was upregulated to 166%, accompanied by a comparable increase in AT1-receptor d. Hypercholesterolemia is associated with AT1-receptor upregulation, endothelial dysfunction, and increased NADH-dependent vascular O₂^{·-} production. The improvement of endothelial dysfunction, inhibition of the oxidase, and reduction of early plaque formation by an AT1-receptor antagonist suggests a crucial role of angiotensin II-mediated O₂^{·-} production in the early stage of atherosclerosis.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:109777 CAPLUS

DOCUMENT NUMBER: 133:26646

TITLE: Effects of Alacepril and Amlodipine on the renal injury induced by a high-cholesterol diet in rats

AUTHOR(S): Atarashi, Keiichiro; Takagi, Masao; Minami, Mayumi; Ishiyama, Akihiro

CORPORATE SOURCE: The Second Department of Internal Medicine, Faculty of Medicine, University of Tokyo, Tokyo, 113-0033, Japan

SOURCE: Journal of Hypertension (1999), 17(12, Pt. 2), 1983-1986

CODEN: JOHYD3; ISSN: 0263-6352

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: A high-cholesterol (HC) diet increases blood pressure and induces renal injury in rats. The authors compared the effects of Alacepril, an ACE inhibitor, and Amlodipine, a Ca antagonist, on the renal injury induced by an HC diet in rats. Design and Methods: Male Sprague-Dawley rats were given either an HC diet only (n = 5), an HC diet and Amlodipine (n = 10), or an HC diet and Alacepril (n = 10). The control rats (n = 5) were given a normal diet. Systolic blood pressure (SBP) was measured by a tail-cuff method. Serum lipids, malondialdehyde (MDA) as a parameter for lipid peroxidn., and urinary protein excretion

were determined at 0, 4, and 8 wk. The renal injury was evaluated histol. by the glomeruli sclerosing score. Results: The HC diet increased SBP. Amlodipine lowered SBP more significantly than Alacepril. Serum total cholesterol was increased by the HC diet and was not affected by either anti-hypertensive agent. HDL-cholesterol was similarly decreased in the 3 HC diet groups. Alacepril, but not Amlodipine, completely attenuated the MDA elevation induced by the HC diet. Urinary protein excretion was decreased by the 2 anti-hypertensive agents at a similar rate. The renal histol. injury assessed by the sclerosing score was ameliorated more significantly by Alacepril than by Amlodipine. Conclusions: Both Amlodipine and Alacepril decreased blood pressure and urinary protein, and ameliorated the renal injury induced by the HC diet in rats. The renal effect of Alacepril seems to be mediated by the decrease in oxidative stress as well as by reduction of blood pressure, since Alacepril lowered the sclerosing score more than Amlodipine and completely attenuated MDA, although the blood pressure reduction by Alacepril was less than that by Amlodipine.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:284651 CAPLUS

DOCUMENT NUMBER: 129:62733

TITLE: Reduction in infarct size by chronic amlodipine treatment in cholesterol-fed rabbits

AUTHOR(S): Hoshida, Shiro; Yamashita, Nobushige; Kuzuya, Tsunehiko; Hori, Masatsugu

CORPORATE SOURCE: First Department of Medicine, Osaka University School of Medicine, Suita, 565, Japan

SOURCE: Atherosclerosis (Shannon, Ireland) (1998), 138(1), 163-170

CODEN: ATHSBL; ISSN: 0021-9150

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Calcium (Ca)-dependent factors, including cholesterol-induced changes in membrane Ca permeability and Ca deposition into lesions, may contribute to plaque formation and stability during the early and late stages of atherogenesis. Amlodipine can reduce atheroma formation in cholesterol-fed rabbits and may be cardioprotective. The authors therefore examined the effects of chronic amlodipine treatment (5 mg/kg daily for 10 wk, p.o.) on infarct size after 30-min coronary occlusion/48-h reperfusion in rabbits fed a diet with or without 1% cholesterol. Infarct size was significantly larger in cholesterol-fed rabbits (72.0%) than in normal-fed rabbits (47.1%). Amlodipine treatment effectively reversed the infarct size augmentation in cholesterol-fed rabbits (46.3%), but did not affect infarct size in normal-fed rabbits (51.0%). In both cholesterol-fed and normal-fed rabbits, Ca content and leukocyte accumulation as assessed by myeloperoxidase activity were significantly higher in the ischemic myocardium than in the nonischemic myocardium. However, Ca content and leukocyte accumulation were markedly elevated in the ischemic myocardium of cholesterol-fed rabbits compared with normal-fed rabbits. Amlodipine treatment effectively reversed this elevation. Acetylcholine showed a marked reduction in endothelium-dependent relaxation in the aorta of cholesterol-fed rabbits, which also was reversed by amlodipine treatment. These results indicate that chronic amlodipine treatment reduces infarct size only in cholesterol-fed rabbits.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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